REMARKS

Claims 1-12, 24, 26 and 28 are pending in the present application. Claim 1 has been amended to include a dispensing device, which contemplates pouring. This does not include a mechanical spray pump means. Basis for this amendment can be found on page 6, lines 22-23 of the specification. Claims 24, 26 and 28 have been amended to clearly define the method of administration as swallowing and to indicate the form of the composition as an aqueous, flowable liquid. The basis for these amendments is found on page 18, lines 5-7, page 19, lines 2-3, and page 2, line 12 of the specification.

35 U.S.C. Section 103(a) Rejection

Claims 1-12, 24, 26, and 28 are rejected under 35 U.S.C. §103(a) as being unpatentable over Boltri, EP 0 733 357. Applicant traverses this rejection under the following basis.

The Examiner asserts that nothing in the Boltri reference teaches away from administration of the composition orally, through the use of a nebulizer. However, to support an obviousness rejection, the prior art must be considered as a whole and must teach or suggest all the claim limitations. *See Hodosh v. Block Drug Company, Inc.,* 786 F.2d 1136, 1143 n.5 (Fed. Cir. 1986). First, Boltri does not teach topical oral administration, generally, but was very specific as to the location of delivery. Nothing in Boltri teaches or suggests modification of the Boltri composition to an oral dosage form, as contemplated by the present invention, and there is no motivation to do so. In fact, the Boltri reference does teach away from oral administration of the composition. Boltri only contemplates compositions for "...topical administration on the skin, also for the vaginal, nasal, otological administration..." (Boltri page 3, lines 15-17). Boltri teaches nothing about administration from the oral cavity.

Boltri teaches a high viscosity, nearly semi-solid, composition that is destructurated by a mechanical means. Specifically, Boltri discloses a nearly semi-solid, topical gel formulation that is sprayed and nebulized through the use of a mechanical pump. *See Boltri* at page 2, lines 3-4. Boltri focuses solving two specific problems. Boltri teaches a composition that can be readily sprayed, but that does not leak from a spray device. Boltri desires that the composition will not spread once applied to the intended surface. To address these problems Boltri teaches that the composition, after removal of the applied mechanical stress, quickly returns to its near semi-solid or gelatinous state and pre-nebulization viscosity. *See Boltri* at page 2, lines 23 and 41. One would expect that a thixotropic formulation as

described by Boltri would produce unacceptable aesthetics for use as a non-nebulized, swallowable composition because without application of a significant mechanical stress (nebulization) the formulation would remain too thick to be acceptable for administration by swallowing. One also may expect that oral administration through nebulization of Boltri's formula would render unacceptable aesthetics also as the quick return to a near semi-solid, gel state after removal of the mechanical stress could cause gagging.

In addition, Boltri teaches that spreading of the gel, once applied, is not desirable. Boltri specifically states that in loco persistence is particularly important. This teaches away from spreading and coating of the alimentary tract as envisioned by the present invention. Thus, there is no motivation to modify the Boltri formulation to a flowable, liquid composition because one of skill in the art would understand that the properties disclosed in Boltri would make said composition unacceptable for administration to the alimentary canal by swallowing and would not render adequate spreading and coating on the alimentary tract.

In contrast, the presently claimed invention is a swallowable liquid that provides good mucoadhesion. The present invention takes the form of a shear thinning, liquid composition; that is, when a small stress is applied (e.g. from pouring or shaking) the present composition thins into a pourable liquid that can adequately spread and coat the alimentary tract and can thus be readily swallowed. No applied mechanical nebulizing stress is required as in the Boltri formulation. Boltri characterizes his disclosed invention as exhibiting pseudoplasticity; i.e., the viscosity decreases with the increase in the intensity of the applied stress. *See Boltri* at page 2, line 40. Thus, one of ordinary skill would not expect that substitution of the mechanical nebulizing stress by mere pouring or shaking (and the addition of an acceptable aqueous, swallowable, liquid carrier) would result in shear thinning properties suitable for a swallowable oral composition with good coating properties. The mucoadhesive formulations of the present invention comprise colloidal suspensions that form a coating matrix on the epithelium of the alimentary canal or the gastrointestinal tract. Upon mixing with the gastrointestinal fluid, the viscosity of the formulation is greater than the viscosity of either the formulation prior to mixing or the gastrointestinal lining fluid alone, thereby achieving good mucoadhesion. There is no motivation or suggestion in Boltri that would cause one of ordinary skill in the art to modify the Boltri composition or route of administration in order to achieve these mucoadhesive effects by delivery to the gastrointestinal tract through oral administration by swallowing.

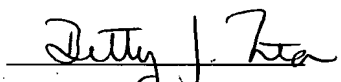
In short, Boltri relates to a topical, near semi-solid, composition with thixotropic properties. There is no suggestion that the Boltri composition could be modified to create an acceptable aqueous swallowable oral liquid composition with good mucoadhesion properties or could be used orally in the manner of Claims 24, 26 and 28. In fact, Boltri teaches away from the modification of the composition to achieve coating of the alimentary tract through administration by swallowing. Therefore, Boltri does not render the present invention obvious under 35 U.S.C. §103(a). Applicant respectfully requests reconsideration and withdrawal of this rejection.

CONCLUSION

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "Version with markings to show changes made".

WHEREFORE, consideration of this Continuation Prosecution Application under 37 C.F.R. §1.53(d), of Application Serial Number 09/361,541, filed July 27, 1999, in view of the foregoing amendments and remarks, allowance of Claims 1-28 are respectfully requested.

Respectfully submitted for
DOUGLAS J. DOBROZSI

By 

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claim 1 (twice amended). A mucoretentive, aqueous, liquid, pharmaceutical composition in oral dosage form comprising:

(a) from about 2% to about 50%, by weight of the composition, of colloidal particles of silica;

(b) a safe and effective amount of a pharmaceutical active selected from the group consisting of gastrointestinal agents, analgesics, decongestants, expectorants, antitussives, antihistamines, bronchodilators, topical anesthetics, sensory agents, oral care agents, miscellaneous respiratory agents, and mixtures thereof;

(c) a per oral or oral aqueous carrier; and

(d) a dispensing device suitable for pouring,

wherein the composition has a sedimentation volume ratio of greater than about 0.90 when measured after about 48 hours and a triggered viscosity ratio of at least about 1.2; and wherein the composition is administered by swallowing.

Claim 24 (amended). A method of coating the alimentary canal by administering, by swallowing, a safe and effective amount of the aqueous, liquid composition of Claim 1.

Claim 26 (amended). A method of preventing or treating symptoms of upper respiratory infections or upper respiratory tract tissue irritation or damage, by administering, by swallowing, a safe and effective amount of the aqueous, liquid composition of Claim 1.

Claim 28 (amended). A method of administering an active agent to the alimentary canal, by administering, by swallowing, a safe and effective amount of the aqueous, liquid composition of Claim 1.